265 Dipeptidyl Peptidase I as a Serum Marker of Allergic Reactions to Food

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RATIONALE: Although dipeptidyl peptidase I (DPPI) is often considered as an enzyme that acts intracellularly, there is evidence for its release from mast cells upon activation. We have investigated the release of this protease into the circulation during allergic reactions to food.

METHODS: Serum was collected before and after diagnostic challenge to peanut, tree nuts, egg, milk and other foods in children with suspected allergy (n=126). Reactions were scored according to the degree of allergen exposure and severity of symptoms. An ELISA developed for measurement of DPPI (using specific monoclonal antibodies that we have prepared) was employed to determine levels in serum. In addition, concentrations of tryptase, carboxypeptidase, chymase and ACE were measured by specific ELISA.

RESULTS: Serum concentrations of DPPI were increased after challenge in children who presented with symptoms, but not in those who did not. Raised DPPI levels were found in patients with objective symptoms ($p=0.007$), and in particular moderate to severe objective symptoms ($p=0.004$), but not in those with subjective symptoms. Increases in serum tryptase, carboxypeptidase, chymase and ACE were not detected following food challenge. Serum DPPI concentrations after challenge correlated with reaction severity scores ($p=0.015$), and with levels of carboxypeptidase ($p=0.004$) and chymase ($p=0.012$), but not tryptase or ACE. The severity of reactions was also associated with baseline levels of DPPI ($p=0.022$) and carboxypeptidase ($p=0.003$).

CONCLUSIONS: The measurement of serum DPPI may provide useful laboratory evidence in support of an allergic reaction to food.

266 Comparative Safety and Efficacy of Sublingual and Oral Immunotherapy for Milk Allergy

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RATIONALE: To our knowledge, sublingual (SLIT) and oral (OIT) immunotherapy for food allergy have not been compared.

METHODS: Subjects were randomized to SLIT (maintenance dose 7mg/day) or OIT escalation (maintenance dose: OITB 1000mg or OITA 2000mg/day) after DBPCFC and initial SLIT escalation. OFCs were performed after 3 and 14 months of daily dosing. If subjects tolerated an 8 gram OFC, they were challenged after 1 and 6 weeks of milk avoidance.

RESULTS: 29 of 30 children, age 6-17 (40%F, median baseline milk-IgE: 37.8 kUa/L, range 1.1-572kUa/L), reached the maintenance dose. After 3 months of maintenance, median OFC threshold was 940mg (range 40-8140mg) in SLIT, 6140mg (2540-8140mg) in OITB and 8140mg (4140-8140mg) in OITA treated subjects ($p=0.001$ SLIT vs. OIT). 6 children in the SLIT group have completed the final OFC (median threshold: 2540mg, range 540-8140mg); one tolerated a full challenge dose before and after 6 weeks of milk avoidance. The remainder appear to be only minimally desensitized and were switched to OIT. Total symptoms were similar between SLIT (32% of doses) and OIT (30% of doses), but were more severe with OIT (anti-histamines used for 1% of SLIT and 18% of OIT doses). Epinephrine was used twice during SLIT and 4 times during OIT. Titrated-SPT decreased and milk-IgG4 increased in all groups. Milk-IgE decreased only after OIT. Neither change in, nor concurrent value of, milk-IgE or milk-IgG4 predicted food challenge outcome.

CONCLUSIONS: At the doses used, OIT was more efficacious than SLIT in desensitizing to milk but was associated with more frequent adverse events.

267 Predictive Value of Peanut Component Specific IgE in a Clinical Population

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RATIONALE: Peanut component IgE analysis has been suggested as a way to enhance the clinical utility of peanut-specific IgE (PN-IgE) measurements, however, this has not been definitively demonstrated in a clinical population in which the diagnosis of peanut allergy is in question.

METHODS: IgE specific for peanut extract (F13) and components Arah1, Arah2, Arah3, and Arah8 were quantified by ImmunoCAP (Phadia) in 61 children who underwent peanut food challenge between 2003-2010 at the Johns Hopkins Pediatric Allergy Clinic. All had sera within two years of their challenge and a positive PN-IgE ≥0.35 kUa/L.

RESULTS: No significant difference was detected in PN-IgE levels between the 29 failed and 34 passed challenges (median 1.32 kUa/L versus 1.34 kUa/L, $p = 0.50$). IgE anti-Arah2 was significantly elevated in patients who failed in comparison to those who passed challenge (median 1.11 kUa/L versus 0.27kUa/L, $p<0.01$). By contrast, serum IgE anti-Arah8 was higher in patients who passed the challenge (median 1.51 versus 0.02 kUa/L, $p<0.01$). IgE anti-Arah1 and Arah3 levels were not predictive of challenge outcome ($p=0.73$, $p=0.27$). When IgE anti-Arah2 positivity was defined as ≥0.35 kUa/L, 86% who failed challenge were IgE anti-Arah2 positive and 74% who passed were IgE anti-Arah2 negative. With a threshold of ≥0.1 kU/L, Arah2-specific IgE antibody levels correctly identified 94% who passed and 62% who failed challenges.

CONCLUSIONS: Arah2 and Arah8-specific IgE antibody levels predict peanut food challenge outcome. These tests may be useful in determining which patients should undergo peanut food challenge.

268 Clinical Factors And Laboratory Correlates Of Milk Allergy Resolution In A Cohort Of Infants With Milk Allergy (CoFAR)

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RATIONALE: There are few studies on the natural history of milk allergy and most are single site, not longitudinal, and do not include data beyond typical allergy tests.

METHODS: Children aged 3-15 months were enrolled in an observational study with either a convincing history of egg and/or milk allergy with a positive prick skin test (PST) to the trigger food, and/or moderate-severe atopic dermatitis and a positive PST to milk or egg. Here, we report on the longitudinal follow-up of children enrolled with a clinical history of milk allergy, with resolution determined by successful ingestion.

RESULTS: Among 244 subjects who were milk allergic at baseline, 89 had resolution of their allergy by month 30 of follow-up, with a Kaplan-Meier probability of milk allergy resolution of 36.9%. The median age at resolution was 24 months. Resolution of milk allergy was associated with lower baseline milk IgE (median 0.72 kU/L for subjects with resolution versus 6.99 kU/L; 65.3% resolution for subjects with IgE <2 kU/L versus 14.2% for IgE ≥5 kU/L), smaller baseline milk PST wheal size (median 5.0mm versus 9.25mm), and mild/none versus moderate/severe baseline atopic dermatitis (Cox regression analysis, all $P<0.001$). Baseline milk-IgG and IgG4 were not predictive of resolution, nor were the casein-stimulated mononuclear cell (CD25-selected) PCR-based screening for expression of CISH, FOXP3, GATA3, IL-10, IL-4, IFN-gamma or TBET.

CONCLUSIONS: In this cohort of infants with milk allergy, about one third had resolved over 30 months of follow-up. Baseline milk-IgE and PST wheal size were the best predictors of the likelihood of resolution.